Contemporary Patterns of Antibiotic Resistance in Humans

By Ron Jones, M.D.
Primary Investigator, SENTRY Program

Antibiotic resistance in humans is growing around the world, but a global collection of human and animal resistant strains shows little significant association between animal and human patterns.

While antibiotic resistance is a public health threat around the world, it is clear that hospital- and community-acquired diseases, unrelated to animal drug use, constitute the major problems. Surveillance data clearly show a disconnect between antibiotic resistance patterns in humans and animals, calling into question the alleged link between resistant bacteria in animals and those in humans. The data also affirm that outbreaks of resistant bacteria are generally local, clearly suggesting that management responses should be local, usually at the ward or medical center level and dominantly attributed to patient-to-patient dissemination or related to flawed infection control practices.

The SENTRY Antimicrobial Surveillance Program, which since 1997 has analyzed worldwide data from the collection of human and animal isolates of bacterial strains, has documented the growing antibiotic resistance problem around the world.[1] The SENTRY Program also provides useful data for evaluating the extent of current resistance threats among human pathogens and any potential correlation or link between use of antibiotics in animals, and the extent of emerging antibiotic resistance in humans.

Current Resistance Concerns in Human Practice. Of the over two million hospital-acquired infections per year in the United States, the resistant organisms of greatest risk for poor patient therapeutic outcomes are:

1. Methicillin-resistant staphylococci especially *S. aureus*;
2. Enterococci resistant to vancomycin or "so-called VRE";
3. *E. coli* and *Klebsiella* spp. resistant to "third-generation" cephalosporins;
4. Most prevalent human clinical pathogens evolving toward resistance to ciprofloxacin and other fluoroquinolones; and
5. Multi-drug resistance among *P. aeruginosa* and *Acinetobacter* spp.

Without exception, none of these problems are related to food-borne pathogens or documented to have contributed significant risk to patients. Rates of resistance among monitored institutions vary widely, but clear increases in resistance among the five (5) listed nosocomial organism resistance problems are driven by use of antimicrobials in humans and other factors that are headed by a decline in the Public Health infrastructure and local infection control practices.

Results from North America for the enterococci continue to see higher resistance rates each year (17%, SENTRY Program for 2001), in an area where no selecting agent exists in animal practice. Similarly, Synercid-resistant strains continue to emerge in North

America and Europe, the latter where the animal product (virginamycin) was removed from use, but pristinomycin remains utilized in human practice (decades prior to Synercid release). Epidemic occurrences of vancomycin- and Synercid-resistant strains continue to occur in Europe, North America and now in Latin America driven by selective pressures of human antibiotic treatment and breaks in infection control policies.
Among community-acquired infections, the principal concerns are:

1. Penicillin and erythromycin resistances in *S. pneumoniae* and other streptococci;
2. Methicillin resistance in staphylococcal skin infections;
3. Fluoroquinolone and trimethoprim/sulfamethoxazole resistance in the Enterobacteriaceae causing urinary tract infections; and
4. Resistance among food-borne pathogens, principally *Campylobacter* and *Salmonella*.

Results from the SENTRY Program indicate that invasive *Salmonella* causes only 0.4% of all blood stream infections in the United States, and the resistances to ampicillin (22%), ceftriaxone (1.6%), ciprofloxacin (0.8%) and trimethoprim/sulfamethoxazole (6.3%) remain low and unchanged over the last five years. Fluoroquinolone resistance in *Campylobacter* was documented before and after its use in animal health, but the preferred treatment (macrolides) remains completely effective. Ironically, the susceptibility rates of these pathogens of suspected animal reservoir origin have antibiotic resistance rates that are significantly less than comparable Enterobacteriaceae of human origin especially among pathogens associated with hospital-acquired bacteremias or community-acquired urinary tract infections.

North America

The growing problem of antimicrobial resistance has led to renewed calls to phase out or ban the use of certain antibiotics given to animals. These calls have persisted despite the lack of sufficient evidence demonstrating a significant risk to human health. Indeed, experts have stated that banning antibiotics as growth promoters in animals will not solve or even impact the problem of antibiotic resistance in hospitals.[2] A greater benefit could be achieved by restoring infection control infrastructures and improving public health educational efforts especially in food preparation.

Most Serious Antimicrobial Resistance Problems
Facing Human Medicine in North America

GRAM-POSITIVE COCCI	RISK FROM ANIMAL SOURCES
Staphylococci	
Methicillin or oxacillin	None
MLS_B (Synercid®)	None
Glycopeptides	None
Streptococci	
DRSP and other	None
Enterococci	
Ampicillin and Aminoglycosides	None
Synercid®	None
Glycopeptides	None
Oxazolidinones	None

GRAM-NEGATIVE BACILLI	RISK FROM ANIMAL SOURCES
Enterobacteriaceae *E coli,* Klebsiella spp., etc.	None
***Salmonella* and other food-borne species**	
ESBLs	None
Stably derepressed Amp C (CMY-2, etc.)	Debated[a]
Fluoroquinolones	Debated[a]
Novel β-lactamases	None
P. aeruginosa	
MDR isolates	None
Acinetobacters	
MD isolates	None
Campylobacters	
Macrolides	None
Fluoroquinolones	Debated[b]

a. Resistance rates in humans are higher than in animal strains.
b. Drugs of therapeutic choice have remained active regardless of resistance discovered in animal pathogens.

Recent reports from the Centers for Disease Control and Prevention document a 23% decline in food-borne infections between 1999 - 2001. This decrease was attributed to initiatives in slaughterhouse safety practices, improved agricultural practices at the level of the farm, adherence to new regulations governing fruit and other juices and an expanded food safety education program. Clearly this indicates significant progress on that small proportion of human infections that are derived from animal sources.[3]

References

1. Jones RN, Turnidge J. SENTRY Antimicrobial Surveillance Program. Five Year Summary [Slide Presentation].
2. Acar J, Casewell M, Freeman J, Goossens H, Friis C. Avoparcin and virginiamycin as animal growth promoters: A plea for science in decision-making. Clinical Microbiology and Infections 2000; 6(9):477-482.
3. Cimons M, Food safety progress hailed while concerns remain. ASM News 68:317-318, 2002.